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HAEMATOLOGY IMAGES

The great mimicker: Leukemic presentation of blastic plasmacytoid dendritic cell neoplasm with PVT1::SUPT3H fusion

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A 65-year-old male with a history of treated follicular lymphoma (in remission) noticed a 'sunspot-like' lesion on the left cheek that was diagnosed as blastic plasmacytoid dendritic cell neoplasm (BPDCN): (Figure 1: intradermal diffuse infiltrate of predominantly large neoplastic cells with expression of CD123). He was treated with three regimens (Tagraxofusp, Decitabine/Venetoclax, and BITE CD123-CD33) but progressed with cerebrospinal fluid, multiple lymph nodes (in the neck and periaortic regions), and later peripheral blood (PB) involvement. His PB smear showed leukocytosis (WBC of 26.7 × 10^{12}/L) and numerous large cells (42%) with scant cytoplasm, variably irregular nuclei, fine chromatin, and inconspicuous to one/two nucleoli, resembling acute myeloid leukemia (AML) cells (Figure 2 -top row, Wright/Giemsa stain, original magnification ×1000). The flow cytometric analysis on a PB sample (taken after 3 days of treatment) revealed a small population of neoplastic BPDCN cells [positive for CD4/CD56/CD123/HLA-DR/LILRB1 (ILT3)/CD303, Figure B-bottom row]. Next generation sequencing revealed a *PVT1::SUPT3H* fusion [corresponding to t(6;8)(p21;q24)] and mutations in *ARID1A* (p.Gln2128*, variant allele frequency (VAF) of 69.50%), *IKZF1* (p.Tyr503Ser, 32.4%), *NRAS* (p.Gln61Lys, 32.44%),

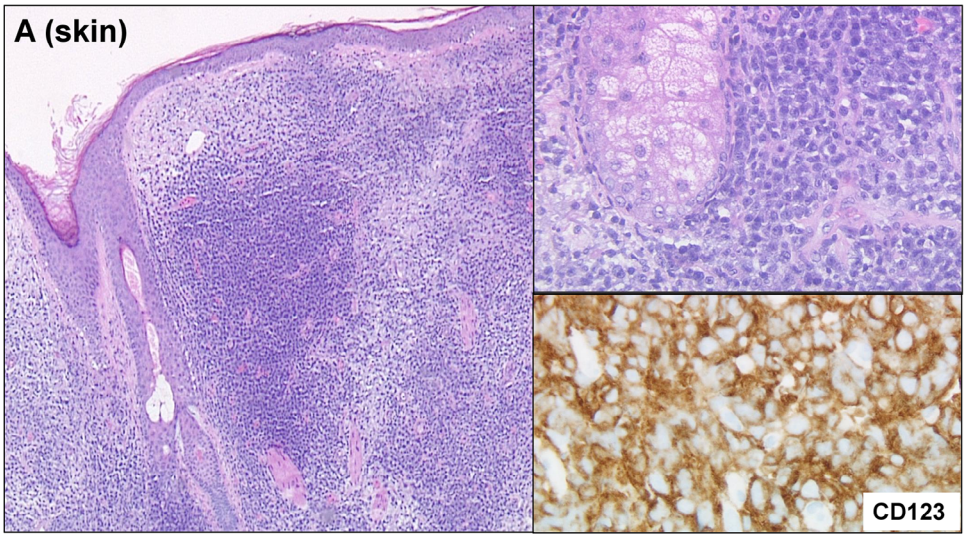

FIGURE 1 Top row, Wright/Giemsa stain, original magnification Ã—1000.

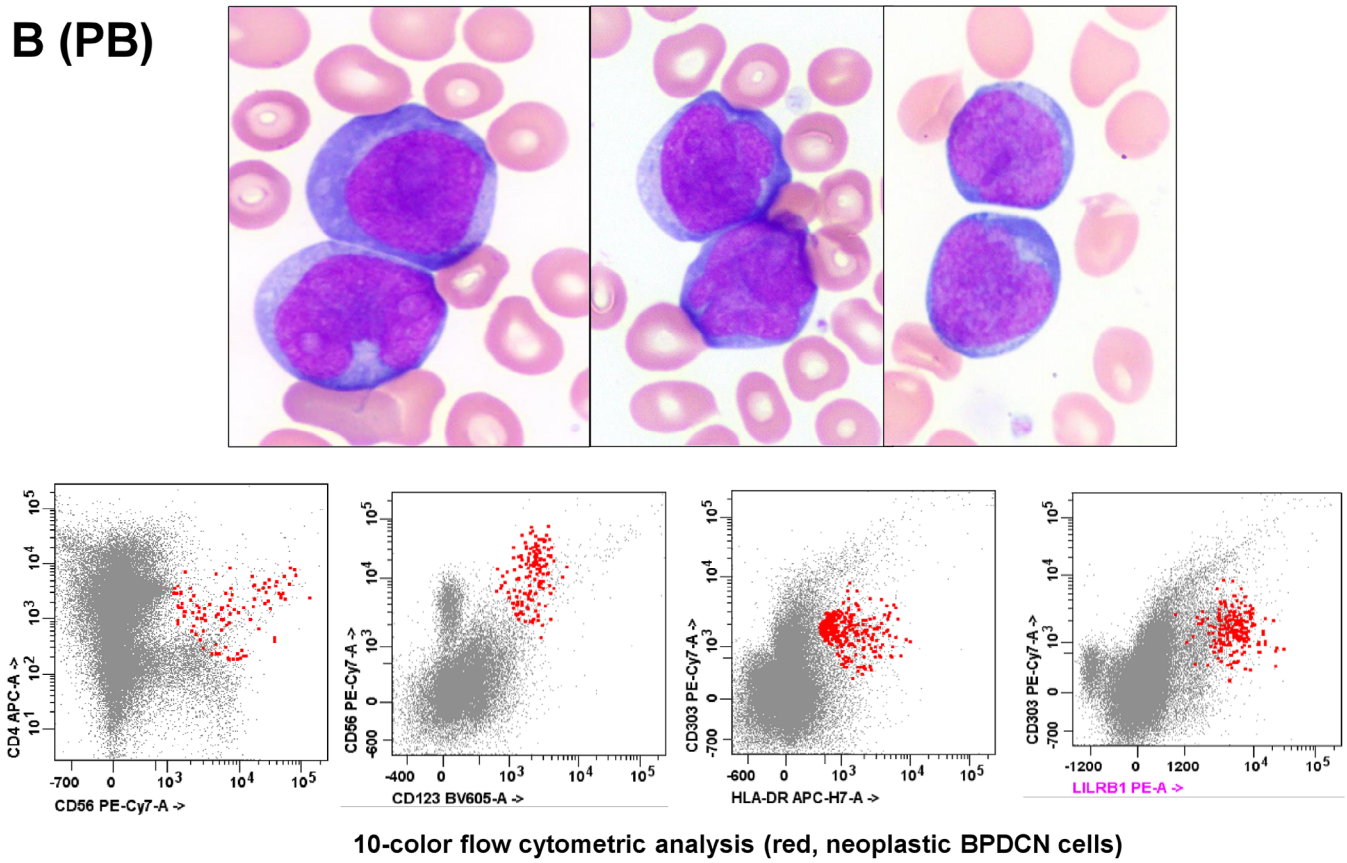

FIGURE 2 Intradermal diffuse infiltrate of large neoplastic cells with expression of CD123.

and *TP53* (p.Gln136Leu, 34.42%). A cytogenetic study was not performed. He was started on HyperCVAD with a resolution of leukocytosis and a bone marrow biopsy performed on day 29 (but not performed at initial leukemic presentation) was negative for tumor infiltrate. However, the disease progressed with the emergence of multiple cutaneous lesions and the patient died 22 months after diagnosis.

BPDCN is a rare and aggressive hematologic neoplasm derived from clonal proliferation of immature plasmacytoid dendritic cells. Herein, we present a rare case of BPDCN harboring an uncommon t(6;8)(p21;q24)/*PVT1*::*SUPT3H* (accounting for 5%–10% of BPDCN), which is characterized by a male predominance, systemic dissemination (involving the skin, PB, and lymph node), and short survival [1, 2], as seen in our patient. Notably, *SUPT3H* on chromosome 6p21 shares a locus with *RUNX2*, and *PVT1* on chromosome 8 is located 149 kb telomeric to *MYC*. Hence, this fusion likely results in *MYC* and *RUNX2* collaboration, promoting the development and progression of BPDCN [3, 4]. Additional cooperative mutations affecting DNA damage, chromatin remodeling, and proliferation detected in our case may further contribute to leukemogenesis. From a diagnostic perspective, BPDCN is a close mimicker of AML and its diagnosis can be challenging while screening the PB smear for acute leukemia due to its rarity and blastic appearance. Our case illustrates that a comprehensive diagnostic work-up including morphologic, immunophenotypic, and molecular assessment is essential in the diagnosis and characterization of this rare neoplasm.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

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N/A

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

ETHICS APPROVAL STATEMENT

The authors have confirmed ethical approval statement is not needed for this submission.

PATIENT CONSENT STATEMENT

The authors have confirmed patient consent statement is not needed for this submission

CLINICAL TRIAL REGISTRATION

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